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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,528	04/27/2006	David Dakin Iorwerth Wright	07588.0081	7494

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EXAMINER	
FISHER, ABIGAIL L	

ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,528	WRIGHT ET AL.	
	Examiner	Art Unit	
	ABIGAIL FISHER	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/16/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Amendments/Remarks filed on March 16 2009 is acknowledged. Claims 1, 4, 6-8, 11-12 and 14-17 were amended. Claims 1-22 are pending.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 3/16/09 was considered by the examiner.

Claim Objections

The objection of claim 17 is **withdrawn** in light of Applicants' amendments filed on March 16 2009).

Modified Rejection based on Amendments filed on March 16 2009

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 as currently written is vague and indefinite. The claim, which depends from claim 1, recites that the gas phase is 100% by volume oxygen. However, claim 1 recites that 0.001 to 0.8% by volume of nitrogen. Therefore it is indefinite as to how the

gas phase is 100% by volume oxygen when a certain percentage is required to be nitrogen.

Response to Arguments

Applicants argue that their amendment has overcome the rejection of claim 8 under 35 USC 112 second paragraph as the term "substantially" has been removed. While the examiner agrees that removal of the term "substantial" overcomes the previous rejection, the amendment results in the claim still being indefinite for the reasons set forth above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tessari (US PGPUB No. 20020077589, cited on PTO Form 1449) in view of Osman et al. (WO 00/72821, cited on PTO Form 1449).

Applicant Claims

Applicant claims a method of making a foam comprising providing two syringes wherein one syringe is charged with a liquid phase and the other with a gas phase or both syringes are charged with the liquid and gas phase. Then the liquid phase and gas phase are transferred repeatedly between the syringes via a connector to form a foam wherein the liquid phase comprises at least one sclerosing agent and the gas phase consisting essentially of gaseous nitrogen present in an amount ranging from 0.0001% to 0.8% by volume and at least one physiologically acceptable gas.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Tessari is directed to a method and apparatus for producing an injectable foam. As claimed a injectable foam is produced comprising a first syringe containing a gas

and a second syringe containing a liquid. The foam is produced by passing the gas and the liquid back and forth between the two syringes (claim 1). The liquid comprises a sclerosant (claim 2). The syringes are attached to a valve to allow for communication between the two syringes (claim 5). Gases taught as suitable include air, oxygen, carbon dioxide, helium or mixtures (paragraph 0007). The gas can be sterilized before or after it is filled into the syringe (paragraph 007). Typical bubble sizes are up to 100 μm (paragraph 0051). It is taught that to pass the gas and liquid back and forth a plunger of one of the syringes is depressed to transfer air into the syringe with the liquid and then the second syringe's plunger is depressed to transfer the air and sclerosant back into the first syringe (paragraph 0047). An apparatus is claimed comprising a first syringe, a second syringe and a valve, in which the firs syringe contains a gas and the second contains a liquid which comprises a sclerosant (claims 17-20).

Ascertainment of the Difference Between Scope the Prior Art and the Claims *(MPEP §2141.012)*

Tessari does not teach that the gas comprises nitrogen. Tessari does not teach a mesh comprising apertures with a maximum dimension ranging from 1 to 200 microns. However, these deficiencies are cured by Osman et al.

Osman et al. is directed to the generation of a microfoam. It is taught hat a problem in using air as a gas for producing a sclerosing microfoam is the perception that large volumes of nitrogen should not unnecessarily be introduced into patient as gas embolism with nitrogen remains a possibility (page 3, lines 6-9). It is taught that passing a stream of sclerosant liquid and gas through one or more passages of 0.1 microns to 30 microns provides a stable blood dispersible gas based sclerosant

injectable microfoam (page 9, lines 16-20). These passages are taught as being provided by openings in a mesh or screen (page 11, lines 1-7). It is taught that a syringe device comprising the gas and liquid can be pushed through these passages via the plunger to convert a foam into a microfoam (column 18, lines 10-16). It is taught that the microfoam when passed between two chambers via the meshes renders a microfoam that is more uniform in nature (page 27, lines 19-20). Gas mixtures taught as suitable includes less than 40% v/v nitrogen and at least 50% oxygen or carbon dioxide up to 100% oxygen or carbon dioxide (page 22, lines 3-14).

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Tessari and Osman et al. and utilize a mesh to pass the foam through. One of ordinary skill in the art would have been motivated to utilize a mesh in the syringe in order to produce a microfoam and one that is more uniform in nature as taught by Osman et al.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Tessari and Osman et al. and utilize smaller amounts of nitrogen in the gas phase. One of ordinary skill in the art would have been motivated to utilize less nitrogen as it is known that in the art that large volumes of nitrogen should not be introduced due to gas embolism as taught by Osman et al.

Regarding the amount of nitrogen present in the gas phase, Osman et al. teach nitrogen in amounts less than 40%. This includes amounts all the way to 0%. One of

ordinary skill in the art would have been motivated to utilize nitrogen in low amounts based on the teachings of Osman et al. It would have been obvious to one of ordinary skill in the art at the time of the invention to engage in routine experimentation to determine optimal or workable ranges for nitrogen that produce expected results. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. **In re Aller, 220 F. 2d 454, 105 USPQ 233 (CCPA 1955).**

Regarding the claimed amounts of oxygen, Tessari tech that the gas phase can comprise oxygen and Osman et al. teach suitable amounts of oxygen. It would have been obvious to one of ordinary skill in the art at the time of the invention to engage in routine experimentation to determine optimal or workable ranges for the oxygen that produce expected results. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. **In re Aller, 220 F. 2d 454, 105 USPQ 233 (CCPA 1955).**

Regarding claims 17-22 directed to a sterile pack, Tessari teaches an apparatus comprising the syringes, liquids, and gas phases. It would have been obvious to one of ordinary skill in the art to combine the teachings of Tessari and Osman et al. and utilize a sterile pack for the apparatus. One of ordinary skill in the art would have been motivated to utilize a sterile pack in order to package and ship the formulation as well as to provide instructions for a consumer/provider on how to utilize the product.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the

instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicants argue that (1) the prior art teaches away from foams comprising very little (removing essentially all) nitrogen from the sclerosing foams. Applicants argue that practitioners believed that by simply lowering the amount of foam injected they could ensure the safety of the procedure. Applicants submit several articles in the art for the examiner to read. It is argued that practitioners believed at the time that polidocanol is the main cause of the side effects and therefore by injecting less foam would lower the amount of polidocanol and therefore lower the risks. Applicants argue that (2) they have submitted a reference, Eckmann et al., which reports a side-by-side comparison in rates of (a) an air based foam, (b) a foam with 7% nitrogen, and (c) a foam with 0.01 to 0.8% nitrogen. The study showed that injection of a foam containing 0.01 to 0.8% nitrogen results in virtually no observable bubbles as compared to foams comprising 80% nitrogen (air) or 7% nitrogen. This displays the unexpectedness of the range of 0.01 to 0.8% by volume of nitrogen.

Applicants' arguments filed March 16 2009 have been fully considered but they are not persuasive.

Regarding Applicants first argument, the examiner has read the documents submitted by applicants. Firstly, polidocanol is not the only sclerosing agent taught in the prior art, STS (sodium tetradecylsulphate), ethanolamine oleate and sodium

morrhuate. Therefore, arguments to polidocanol would not apply to the other sclerosing agents. Furthermore, in Tessari et al. STS appears to be a preferred sclerosing liquid. Secondly, there is nothing in the instant claims that would preclude lower amounts of the sclerosing liquid to be injected. The requirement of the instant claims is the lower amount of nitrogen. Tessari et al. teach that suitable gases include air, oxygen, carbon dioxide, helium and mixtures thereof. Therefore, gas phases could include 100% oxygen, carbon dioxide or helium which would not possess any nitrogen. Therefore, the art does recognize that no nitrogen gases are suitable. Furthermore, Osman et al. teach that a problem that large volumes of nitrogen should not be unnecessarily introduced. Therefore, the art recognizes problems associated with nitrogen. As pointed out by applicants as taught in Osman et al. (page 9) a **preferred** form is 99% or more oxygen with the remainder being carbon dioxide or carbon dioxide, nitrogen and trace gases in the proportion found in atmospheric air. Osman et al. teaches in that same section minor proportion only of nitrogen being preferred. Therefore, the teachings of Osman et al. as a whole teach 99% or more oxygen which would result in 1% or less of other gases such as carbon dioxide and nitrogen. Therefore, Osman et al. teach utilizing low amounts (i.e. less than 1%) of nitrogen.

Regarding applicants second argument, firstly the examiner would like to point out that Eckmann et al. do not disclose the nitrogen content of the gases tested. The only gas wherein the nitrogen content is disclosed is (a) which is comprised of air wherein it is generally known in the art that air comprises 80% nitrogen. Secondly, it is unclear why gases (a) and (b) comprise static amounts of nitrogen whereas (c) does

not. However, assuming that the contents argued by applicants is the same as that in Eckmann et al., this evidence does not show the criticality of the percentage claimed over that of the Osman et al. The study by Eckmann et al. establishes that compared to a 7% nitrogen containing gas that a gas comprising 0.01 to 0.8% nitrogen behaves better. However, as pointed out by applicants and argued above Osman et al. teach 1% or less of a gas other than oxygen, which could be entirely nitrogen. Therefore, the lowest amount of nitrogen taught is 1% or less, which overlaps that instantly claimed. Therefore, the data presented in Eckmann et al. does not establish the unexpectedness of 0.8% nitrogen over what is taught in Osman et al. which is 1% or less.

Therefore, the rejection is maintained since applicant has not provided any persuasive arguments to overcome the rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 and 10-12 copending Application No. 10432328 in view of Osman et al. (WO 00/72821). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims overlap in scope.

The instant application claims a method of making a foam comprising providing two syringes wherein one syringe is charged with a liquid phase and the other with a gas phase or both syringes are charged with the liquid and gas phase. Then the liquid phase and gas phase are transferred repeatedly between the syringes via a connector to form a foam wherein the liquid phase comprises at least one sclerosing agent and the gas phase consisting essentially of gaseous nitrogen present in an amount ranging from 0.0001% to 0.8% by volume and at least one physiologically acceptable gas.

Copending '328 claims a method for producing a microfoam comprising introducing within a twenty-four hour period prior to using the microfoam at least one physiologically acceptable blood-dispersible gas comprising oxygen from a first container into a second container by means of a connector assembly, wherein prior to inducing the gas from the first container, the second container contents comprise a liquid phase comprising at lease one aqueous sclerosant liquid and a gas phase consisting essential of a gas or gas mixture which is inert to the sclerosant liquid and

releasing from the second container a mixture of the blood-dispersible gas and sclerosant liquid where upon release of the liquid a microfoam is produced.

Copending '328 does not claim that the gas contains nitrogen. However, this deficiency is cured b Osman et al.

Osman et al. is directed to the generation of a microfoam. It is taught hat a problem in using air as a gas for producing a sclerosing microfoam is the perception that large volumes of nitrogen should not unnecessarily be introduced into patient as gas embolism with nitrogen remains a possibility (page 3, lines 6-9). Gas mixtures taught as suitable includes less than 40% v/v nitrogen and at least 50% oxygen or carbon dioxide up to 100% oxygen or carbon dioxide (page 22, lines 3-14).

It would have been obvious to one of ordinary skill in the art at time of the instant invention to combine the teachings of copending '328 and Osman et al. and utilize nitrogen in small amounts. One of ordinary skill in the art would have been motivated to utilize small amounts of nitrogen as Osman et al. teach that large volumes of nitrogen should not unnecessarily be introduced into patient as gas embolism with nitrogen remains a possibility. Therefore, one of ordinary skill in the art would have been motivated to utilize nitrogen as it is taught as a suitable gas for use in forming a foam with a sclerosing agent albeit in small amounts. Furthermore, it would have been obvious to one of ordinary skill in the art at the time of the invention to engage in routine experimentation to determine optimal or workable ranges for nitrogen that produce expected results. Where the general conditions of a claim are disclosed in the prior art,

it is not inventive to discover the optimum or workable ranges by routine experimentation. **In re Aller, 220 F. 2d 454, 105 USPQ 233 (CCPA 1955).**

Therefore, the scopes of the copending claims and the instant application overlap and thus they are obvious variants of one another.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicants argue that for the same reasons as stated above, Osman et al. does not cure the deficiencies of copending Application 10/432328.

Applicants' arguments filed March 16 2009 have been fully considered but they are not persuasive.

Regarding applicants arguments, as indicated above Osman et al. teach gas content of 99% or more of oxygen, which would result in 1% or less of other gases such as nitrogen. Osman et al. teach incorporation of minor amounts of nitrogen in the gas phase. Therefore, Osman et al. teaches one of ordinary skill in the art that not only are large amounts of nitrogen not advisable but teaches preferred amounts comprise 1% or less of nitrogen. Therefore, the rejection is maintained since applicant has not provided any persuasive arguments to overcome the rejection.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ABIGAIL FISHER whose telephone number is (571)270-3502. The examiner can normally be reached on M-Th 9am-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Abigail Fisher
Examiner
Art Unit 1616

/Johann R. Richter/
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